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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/501,407	03/25/2005	Victor Willem Van Beusechem	253-9	9615
23869 7590 09/28/2009 HOFFMANN & BARON, LLP 6900 JERICHO TURNPIKE SYOSSET, NY 11791				
EXAMINER				
LONG, SCOTT				
ART UNIT		PAPER NUMBER		
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

### Office Action Summary

**Application No.**

10/501,407

**Applicant(s)**

VAN BEUSECHEM ET AL.

**Examiner**

SCOTT LONG

**Art Unit**

1633

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 24 June 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 10,15-17,19-23 and 26-40 is/are pending in the application.
- 4a) Of the above claim(s) 10,15-17,19-23 and 40 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 26-39 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/808)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

### **DETAILED ACTION**

*The examiner acknowledges receipt of Applicant's Remarks, filed on 24 June 2009.*

#### ***Claim Status***

Claims 10, 15-17, 19-23 and 26-40 are pending. Claims 1-9, 11-14, 18, and 24-25 have been cancelled. Claims 10, 15-17, 19-23 and 40 are withdrawn from further consideration by the Examiner, pursuant to 37 CFR 1.142(b), as being drawn to non-elected inventions, there being no allowable generic or linking claim. The claims filed 6/24/2009 contained no amendments. 26-39 are under current examination.

#### ***Priority***

This application claims benefit from foreign Application No. EP/02075108.7, filed 14 January 2002 and PCT Application No. PCT/EP03/00340, filed 14 January 2003. The instant application has been granted the benefit date, 14 January 2002, from the application EP/02075108.7.

**RESPONSE TO ARGUMENTS**

**35 USC § 102**

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 26-27, 34 and 39 remain rejected under 35 U.S.C. 102(b) as being anticipated by Fueyo et al (Oncogene. 2000. 19:2-12) and as evidenced by Nevins (Human Molecular Genetics. 2001. 10(7):699-703) for the reasons of record and the comments below.

The applicant's arguments (Remarks, page 9) have been fully considered but are unpersuasive.

The applicant argues "the adenovirus of Fueyo et al. does not include a coding sequence of at least one mammalian restoring factor functional in restoring the p53 apoptosis pathway, as required by claim 26." Contrary to the applicant's view, Fueyo et al. teach an adenovirus comprising "a coding sequence of at least one mammalian restoring factor functional in restoring the p53 apoptosis pathway" because the specification defines "restoring factor" so broadly as to encompass the teachings of Fueyo. The specification teaches "non-limiting examples of said restoring factor are p53" (page 14, lines 31-32). The specification further teaches, "Thus, 'restoring factor' includes a wild-type factor and all its natural or synthetic derivatives that share at least one activity with said wild-type factor" (page 15, lines 16-18). According to the

specification's definitions regarding "restoring factor," the examiner concludes that the p53 derivative of Fueyo meets the limitations of the instant claims.

The applicant argues (page 10) that Fueyo does not disclose an adenovirus comprising a coding sequence of at least one mammalian restoring factor functional in restoring the p53 apoptosis pathway, as claimed. Contrary to the applicant's assertion, Fueyo teach "an adenovirus comprising a coding sequence of at least one mammalian restoring factor functional in restoring the p53 apoptosis pathway." Fueyo et al. teach a "replication competent" recombinant adenovirus (p.2, *Results*, paragraph 1). Further, Fueyo et al. teach that the virus can "replicate in and lyse cancer cells" (abstract). Their virus "induced cell death even in mutant-p53 cells" (p. 7, *Treatment with Δ24*). This indicates that the Fueyo adenovirus is capable of restoring p53 apoptosis in the target cells hampered in the p53 apoptosis pathway. As mentioned above, the applicant has broadly defined any p53 molecule to be a mammalian restoring factor. Furthermore, Fueyo teaches that their virus (containing a p53 gene) can induce tumor cell death (at least by lysis) in cells that are defective in p53. The instant specification teaches "at late stages of infection cell death and lysis promote release of the virus progeny from the cell. An important mechanism used by adenovirus to accomplish this is through induction of apoptosis" (page 7, lines 12-15). Fueyo shows cells having a defective p53 apoptosis pathway lyse after being infected with replication competent recombinant adenovirus containing the (restoring factor) p53 gene. The adenovirus of Fueyo satisfies the structural limitations of the instant claims and seems to show the inherent

properties of the claim limitations. Therefore, the examiner finds the applicant's argument unpersuasive.

Therefore, the examiner hereby maintains the rejection of claims 26-27, 34 and 39 remain rejected under 35 U.S.C. 102(b) as being anticipated by Fueyo et al (Oncogene. 2000. 19:2-12) and as evidenced by Nevins (Human Molecular Genetics. 2001. 10(7):699-703).

The examiner reiterates the pending rejection:

Claims 26-27, 34 and 39 are rejected under 35 U.S.C. 102(b) as being anticipated by Fueyo et al (Oncogene. 2000. 19:2-12) and as evidenced by Nevins (Human Molecular Genetics. 2001. 10(7):699-703).

Claim 26 is directed to a replication competent recombinant adenovirus, being capable to replicate and having lytic capacity in target cells, wherein said target cells are hampered in a p53 dependent apoptosis pathway, wherein the adenovirus is a conditionally replicating adenovirus; wherein the adenovirus genome comprises a coding sequence of at least one mammalian restoring factor functional in restoring the p53 apoptosis pathway in said target cells; wherein said coding sequence is operably linked to one or more expression control sequences functional in said target cells, and whereby said restoring factor induces accelerated cell lysis and/or a faster release of virus progeny when compared to a recombinant adenovirus lacking said coding sequence.

Fueyo et al. teach a "replication competent" recombinant adenovirus (p.2, *Results*, paragraph 1). Further, Fueyo et al. teach that the virus can "replicate in and

lyse cancer cells" (abstract). Their virus "induced cell death even in mutant-p53 cells" (p. 7, *Treatment with  $\Delta 24$* ). This indicates that the Fueyo adenovirus is capable of restoring p53 apoptosis in the target cells hampered in the p53 apoptosis pathway. Additionally, Fueyo et al. indicate that their adenovirus can "express a mutant E1A protein" (p.3). Consequently, the p53 apoptosis pathway is restored by expression of the mutant E1A protein. The Fueyo adenovirus replicates conditionally, "this mutant virus would be selective for tumors...most normal...cells halts...the replication of the mutant adenovirus...this adenovirus would also be able to replicate in cancer cells...but not the surrounding differentiated cells" (p.2, *Introduction*). The instant claim also contains the limitation, "whereby said restoring factor induces accelerated cell lysis and/or a faster release of virus progeny when compared to a recombinant adenovirus lacking said coding sequence." The examiner does not believe this phrase should be given patentable weight because the limitation is included in a "whereby clause" (see MPEP 2106). Fueyo may not have made the comparison between their adenovirus and "a recombinant adenovirus lacking said coding sequence," but the structure of the Fueyo adenovirus satisfies the structural limitations of the instant claim and matches some embodiments provided by the instant specification. The specification teaches "non-limiting examples of said restoring factor are p53" (page 14, lines 31-32). The specification further teaches, "Thus, 'restoring factor' includes a wild-type factor and all its natural or synthetic derivatives that share at least one activity with said wild-type factor" (page 15, lines 16-18). According to the specification's definitions regarding

"restoring factor," the examiner concludes that the p53 derivative of Fueyo meets the limitations of the instant claims.

Claim 27 is directed to the adenovirus of claim 26 wherein said adenovirus is a "human adenovirus." Fueyo et al. teach "the replication-competent  $\Delta 24$  virus is a human adenovirus 5" (p. 2).

Claim 34 is directed to the adenovirus of claim 26 wherein a mutation in a E1A region encompassing at least part of the pRb-binding CR2 domain of E1A. Fueyo et al, "constructed a tumor-selective adenovirus,  $\Delta 24$ , that carries a 24-bp deletion in the *E1A* region responsible for binding Rb protein." (abstract). The art indicates the pRb-binding CR2 domain of E1A is longer than 24 amino acids. Therefore, the mutant E1A region of Fueyo comprises at least part of the pRb-binding CR2 domain. The "link between the Rb/E2F pathway and the p53 response" is taught by Nevin (p.700).

Claim 39 is directed to the adenovirus of claim 27 wherein said human adenovirus is a serotype 5 adenovirus. Fueyo et al. teach "the replication-competent  $\Delta 24$  virus is a human adenovirus 5" (p. 2).

Accordingly, Fueyo et al. anticipated the instant claims.



***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 26-33 and 35-39 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Chang et al. (US-6,638,762) in view of Lin et al. (Cancer Research. Oct 15, 2000. 60. p.5895-5901) for the reasons of record and the comments below.

The applicant's arguments (Remarks, page 10-14) have been fully considered but are unpersuasive.

The applicant argues (Remarks, page 11) neither Lin et al. or Chang et al. disclose the adenovirus genome comprises a coding sequence of at least one mammalian restoring factor functional in restoring the p53 apoptosis pathway in said target cells. Lin et al. teach that their adenovirus comprising mutant p53 14/19 restores function in cells "which lack endogenous p53" (Transcriptional Activation, p. 5896) and "induce...apoptosis at similar levels to adenovirus *wt*-p53" (Transcriptional Activation, p.5896). Therefore, Lin et al. teach an adenovirus which contains a restoring factor. Therefore, the examiner finds the applicant's argument unpersuasive.

The applicant further argues (Remarks, page 12) that the examiner used hindsight reasoning to arrive at the claimed invention. In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

The applicant also argues (Remarks, page 12) that a skilled artisan would not have had a reasonable expectation of success in combining Lin and Chang. The applicant has submitted a review article (not included in an IDS) with his remarks to

support his reasoning that there was no expectation of success in combining the cited references. The review article is Hermiston et al. (Gene Therapy. 2002; 9: 1022-1035). The applicant has suggested that in view of Hermiston page 1026, a skilled person would never incorporate the sequence which would attenuate virus replication into a replication competent virus. While not explicitly stated, the examiner interprets this to mean that as p53 causes cell lysis and apoptosis in tumor cells defective in p53, that a skilled artisan would not incorporate p53 into a replication competent adenovirus for use in treating cancer. Both the applicant and the examiner know that p53-Adenovirus vectors have been used for years in gene therapy methods for treating cancer. It is evident from both Lin and Chang and the much literature discussed during the course of the multi-year prosecution of this application that p53 can and is used in replication competent recombinant adenoviruses. Accordingly, the examiner concludes that a skilled artisan would be aware of such literature (including Lin and Chang) and motivated to combine the teachings of Lin and Chang and would successfully create a replication competent recombinant AdV-p53 vector.

The applicant reminded the examiner (Remarks, page 13, last parag.) of his rejection of (now cancelled) claims 5, 6 and 8 under lack of enablement found in the Action (filed 7/31/2006). The applicant suggests that the examiner's conclusions in 7/31/2006 regarding the lack of enablement of vectors having E1B-55kDa, E1B-19kDa or E4orf6 proteins indicate that a vector resulting from "the combination of Lin and Chang would not work." According to the subsequent action (filed 3/21/2007), the examiner accepted the applicant's argument that vectors having E1B-55kDa, E1B-

19kDa or E4orf6 proteins would work. Therefore, the examiner finds the applicant's argument unpersuasive. At the current time, there is no lack of enablement rejection pending. Therefore, the examiner finds this argument unpersuasive.

Therefore, the examiner hereby maintains the rejection of claims 26-33 and 35-39 under 35 U.S.C. 103(a) as being unpatentable over Chang et al. (US-6,638,762) in view of Lin et al. (Cancer Research. Oct 15, 2000. 60. p.5895-5901).

The examiner reiterates the pending rejection:

Claims 26-33 and 35-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chang et al. (US-6,638,762) in view of Lin et al. (Cancer Research. Oct 15, 2000. 60. p.5895-5901).

Claim 26 is directed to a replication competent recombinant adenovirus, being capable to replicate and having lytic capacity in target cells, wherein said target cells are hampered in a p53 dependent apoptosis pathway, wherein the adenovirus is a conditionally replicating adenovirus; wherein the adenovirus genome comprises a coding sequence of at least one mammalian restoring factor functional in restoring the p53 apoptosis pathway in said target cells; wherein said coding sequence is operably linked to one or more expression control sequences functional in said target cells, and whereby said restoring factor induces accelerated cell lysis and/or a faster release of virus progeny when compared to a recombinant adenovirus lacking said coding sequence.

Chang et al. teach many of the limitations of claim 26, including a "cell-specific...recombinant...adenovirus" (abstract) which is "replication competent"

(column 32, line 21), "replication-conditional" (abstract) and can "provide a therapeutic benefit in a tissue...from one or more heterologous gene products expressed from the vector" (abstract).

While Chang et al does not explicitly teach that the target cells are hampered in the p53 dependent apoptosis pathway, Lin et al. teach that their adenovirus restores function in cells "which lack endogenous p53" (Transcriptional Activation, p. 5896) and "induce...apoptosis at similar levels to adenovirus wt-p53" (Transcriptional Activation, p.5896). Therefore, Lin et al. teach an adenovirus which contains a restoring factor.

Claim 27 is directed to the adenovirus of claim 26 wherein said adenovirus is a "human adenovirus." Chang et al teach a "human adenovirus 5" (column 4, line 1).

Claim 28 is directed to the adenovirus of claim 26 wherein said adenovirus is an "early adenovirus gene is controlled by a tumor-specific promoter." Chang et al teach the limitation of claim 28 that "a gene in the adenovirus E1 region is operably linked to the tissue-specific transcriptional regulatory control sequence. Preferably the E1a, E1b, or E2a" (column 7, lines 34-39). Chang et al. further teach the "tumor-specific promoter" (column 7, line 49).

Claim 29 is directed to the adenovirus of claim 26 wherein said adenovirus is a "trans-complemented adenovirus." Chang et al. teach the further limitation of claim 29 that "replication is conditioned upon the presence of a trans-acting transcriptional factor" (Col 5, lines 9-10).

Claims 30-31 are directed to the adenovirus of claim 26 wherein the genome of said adenovirus comprises "E1B-55kDa protein" (claim 30) and "E1B-19kDa protein" (claim 31). Chang et al. teach the limitations of claims 30-31 that "the invention further embodies the use of...vectors having...essential regions...for replication...E1b19 kDa gene, or E1b 55 kDa gene" (column 17, lines 20-23).

Claim 32 is directed to the adenovirus of claim 30 wherein the genome of said adenovirus comprises "genes of the...E4 region." Chang et al. teach the limitation of claim 32, "E4 coding region" (column 17, line 18).

Claim 33 is directed to the recombinant virus according to claim 30, where the virus genome comprises at least the gene encoding the adenovirus E4 or F6 protein or function analogues or derivative thereof. Chang et al. teach "E4 coding region" (column 17, line 18).

Claim 35 is directed to the recombinant virus according to claim 26, wherein the restoring factor is p53 protein or a function al analogue or derivative thereof. Lin at al. teach an adenovirus "p53 variant (p53 14/19) containing double substitutions at amino acid residues Leu-14 and Phe-19... p53 14/19 is deficient in mdm2 binding" (Results, p.5896).

Claim 36 is directed to the recombinant virus according to claim 35, wherein the protein lacks a functional binding domain for a human Mdm2 protein. Lin at al. teach an adenovirus "p53 variant (p53 14/19) containing double substitutions at amino acid

residues Leu-14 and Phe-19... p53 14/19 is deficient in mdm2 binding" (Results, p.5896).

Claim 37 is directed to the recombinant virus according to claim 35, wherein the protein is a functional derivative of human p53 with mutated amino acids Leu-14 and Phe-19. Lin et al. teach an adenovirus "p53 variant (p53 14/19) containing double substitutions at amino acid residues Leu-14 and Phe-19... p53 14/19 is deficient in mdm2 binding" (Results, p.5896).

Claim 38 is directed to the adenovirus of claim 26 wherein the target cell is a human cell chosen from the group consisting of cancer cells, arthritic cells, smooth muscle cells, and cells infected with a virus. Chang et al. teach the limitation of claim 38 that the target cells are "tumors, ...arthritis" (column 23, lines 50-57), and "tumor types include...soft tissue...reproductive tract" (column 23, lines 47-48). Vascular smooth muscle cells are an inherent sub-type of soft tissue. The tumors of the reproductive tract include cervical cancer which is commonly caused by human papilloma virus. Chang et al. teach activation of their tissue specific adenoviruses through "transcriptional regulatory factors include...transactivating factors produced by endogenous viral sequences such as from CMV, HIV, EBV, HSV, SV40, and other such viruses that are pathogenic...in humans" (column 9, lines 43-47). Therefore target cells infected with viruses other than the therapeutic adenovirus is taught by Chang et al.

Claim 39 is directed to the adenovirus of claim 27 wherein said human adenovirus is a serotype 5 adenovirus. Chang et al. teach a "human adenovirus 5" (column 4, line 1).

Chang et al. does not teach the limitations of claims 35-37, specifically that the restoring factor is p53 and that the p53 protein lacks a functional MDM2 binding domain and a functional derivative of human p53 mutated with amino acids Leu-14 and Phe-19.

While Chang et al does not explicitly teach that the target cells are hampered in the p53 dependent apoptosis pathway, Lin et al. teach that their adenovirus restores function in cells "which lack endogenous p53" (Transcriptional Activation, p. 5896) and "induce...apoptosis at similar levels to adenovirus *wt*-p53" (Transcriptional Activation, p.5896).

Lin et al. teach an adenovirus "p53 variant (p53 14/19) containing double substitutions at amino acid residues Leu-14 and Phe-19... p53 14/19 is deficient in mdm2 binding" (Results, p.5896). Lin et al. also teach that the adenovirus restores function in cells "which lack endogenous p53" (Transcriptional Activation, p. 5896) and "induce...apoptosis at similar levels to adenovirus *wt*-p53" (Transcriptional Activation, p.5896). Lin et al. does not teach the replication competent adenovirus, but rather a replication defective p53 adenovirus. Lin et al. also do not teach tissue specific conditional replication.

It would have been obvious to a person of ordinary skill in the art at the time of the invention was made to incorporate the tissue specific replication conditional control features of Chang et al into the adenovirus p53 construct of Lin et al. which contains mutations to the MDM-2 binding site of p53.



The person of ordinary skill in the art would have been motivated to make those modifications because "p53 14/19 modified tumor suppressor gene may be a promising therapeutic agent for human cancers that express abnormally high levels of mdm2 oncogene product" (Lin et al., abstract, P.5895). A skilled artisan would have been motivated to incorporate the modifications Lin et al. into the adenovirus of Chang et al., because the adenovirus of Lin et al. is directed to "mdm2 gene amplification in tumor types...soft tissue sarcomas," (Introduction, p.5895). The tissue specific adenovirus of Chang et al. is suited to "tumor types include...soft tissue sarcoma" (column 23, line 47). The combined adenovirus could have enhanced anticancer effects through the addition of the improvements to the known tumor suppressor, p53, and the augmented killing effect created as the replicating virus spread its effect throughout the soft tissue sarcomas.

At the time the invention was made, there would have been a reasonable likelihood of success because the state of the art involving mutagenesis and adenoviruses were commonly practiced.

Therefore the adenoviruses as taught by Chang in view of Lin et al. would have been *prima facie* obvious over the adenovirus of the instant application.

***Conclusion***

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

No claims are allowed.

***Examiner Contact Information***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Scott Long** whose telephone number is **571-272-9048**. The examiner can normally be reached on Monday - Friday, 9am - 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Joseph Woitach** can be reached on **571-272-0739**. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/SDL/ Scott Long  
Patent Examiner, Art Unit 1633

*/Q. JANICE LI/  
Primary Examiner, Art Unit 1633*